REPORT ON THE RESEARCH WORK PERFORMED DURING THE ACADEMIC YEAR 1926-1927, on "THE REACTIONS OF THE BONE MARROW IN ANAEMIA, WITH SPECIAL REFERENCE TO GELATINOUS DEGENERATION".

Submitted for Competition

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THE GUNNING VICTORIA JUBILEE PRIZE,-

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by

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While this investigation was being carried out, an interim report on its progress was submitted to the Examiners for the Degree of B.Sc.Hons. in Pathology. Since then, however, the work has been completed and the present report consequently contains the results of further experiments.

The report comprises:-

A. A short account of the Literature on Gelatinous Degeneration with a list of references.

B. An account of the Examination of Human Bone Marr-:ows removed from the post-mortem room.

C. An account of the work on the Experimental Pro-:duction of Gelatinous Degeneration.

D. Tentative Conclusions drawn from the above three sources (A.B. and C.)

E. Acknowledgments.

A. A SHORT ACCOUNT OF THE LITERATURE ON GELATINOUS DEGENERATION.

Gelatinous Degeneration may be defined as a retro-:gressive change of the bone marrow in which there is a progressive diminution of the haemogenetic tissue accomp-:anied by a change in the fat cells.

The Macroscopic appearances, according to Carnegie Dickson, "may vary almost indefinitely, and depend not so much upon the change itself as upon the previous con-:dition of the tissue in which it occurs, as it may supervene in a normal fatty marrow or in a marrow active-:ly leucoblastic or erythroblastic. Moreover, not all the marrow in the lumen of any one part of any one bone need necessarily take part in the gelatinous degeneration. Typically, the gelatinous part has a glistening homogen-:eous appearance, is translucent and, at times, even transparent. It varies in colour from intensely dark red, through red, light red and yellow to almost colour-:less.

Microscopically, the fat cells are replaced to a greater or lesser extent by a homogeneous eosinophil sub-:stance. Lying throughout the latter are very fine fibrils which show no special arrangement and intertwine with each other frequently. Carnegie Dickson asserts that "it is frequently possible to trace these to the bodies of certain small cells with rounded nuclei, of which/

which they appear to be the processes". He further suggests that these cells are really the remains of the reticular and the fat cells which have undergone myxomat-:ous degeneration. In support of this view, the posit-:ion of the homogeneous substance round the periphery of the fat cells in cases of early gelatinous degeneration, suggests that it may be formed in the cytoplasm of the fat cells by a degenerative process which starts at the periphery of the cell and spreads inwards. In areas in which the above changes have occurred, the haemogen-:etic cells are found in widely-scattered areas and tend to disappear. According to Gulland and Goodall, "the type of cell which preponderates is usually the lympho-:cyte with the representatives of the cellular activity before the gelatinous change supervened".

NOTE: Oedema of the marrow produces an appear-:ance not unlike that of gelatinous degeneration, but microscopically it is seen to be granular and devoid of fibrils.

Apart from the changes just described, Carnegie Dickson describes an acute form of gelatinous degenerat-:ion. The chief differences from the above are :-

1. The clinical course is comparatively extreme-:ly rapid, e.g. three weeks in a case of ulcerative endocarditis.

2. The homogeneous substance is relatively scanty.

3. The fibrillar network replacing the fat is very conspicuous and contains fluid.

Various/

Various views have been expressed regarding the nature of Gelatinous Degeneration. The comparison by Bichat in 1801 to the primitive or embryonic marrow of the foetus (i.e. prior to the fourth month of intra-:uterine life), is unwarranted for the embryonic marrow "is composed of mucoid cells, the branching processes of which form a delicate inter-lacing network resembling that seen in any other mucoid tissue". The branching cells of the primitive or embryonic marrow later form the frame-work of the adult tissue (Van der Stricht, Duval and Stöhr), although Kölliker believes that the branching mucoid cells develop into the marrow proper. Neumann, Bizzozero and Torre consider that the degener-:ation is a change of the fat cells into true myxomatous tissue consisting of mucoid cells in a homogeneous matrix which contains mucin. Roger and Josué, however, could not find the mucin.

Conditions causing, or associated with gelatinous degeneration have been studied. Jackson and others found the condition in association with starvation. They produced it experimentally by starving pigeons and rabbits, and found that it could be completely and rapid-:ly recovered from, by the administration of nourishment.

Gelatinous Degeneration may be primary as in starv-:ation. More commonly, however, it occurs secondarily to exhaustion of the marrow as in prolonged septicaemias and especially ulcerative endocarditis, tuberculosis and Bright's/

Bright's disease (Muir). Presumably, in such chronic infections, the marrow degenerates owing to receiving an insufficient supply of "some essential foodstuff required for cytopoiesis" (Piney).

Apart from its natural occurrence, Stockman and Charteris produced it experimentally by the prolonged administration of lead, mercury, phosphorus and arsenic. Raimondi produced it in rabbits with lead acetate. Nucleic acid, various organisms or their toxins, liver extracts and peptones are capable of producing similar changes (Milroy and Malcolm, Roger and Josué, Haushalter and Spillmann and Robert Muir). Gelatinous degeneration can also be caused experiment-:ally by deficient diets (Piney).

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REFERENCES.

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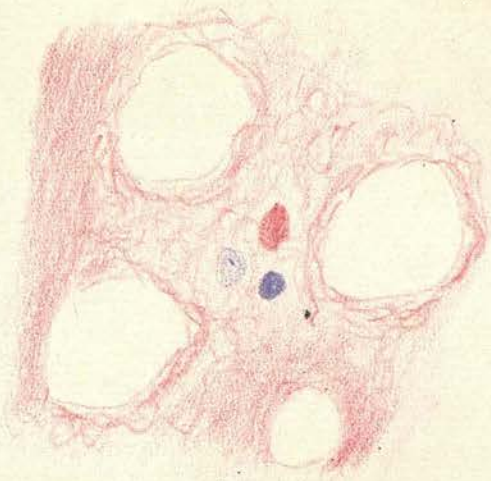


Chronic Gelatinous Degeneration.

Disappearance of haemogenetic cells.

Dense "gelatinous material".

Network of fibrils alternating with "homogeneous interstitial substance".

Acute Gelatinous Degeneration.

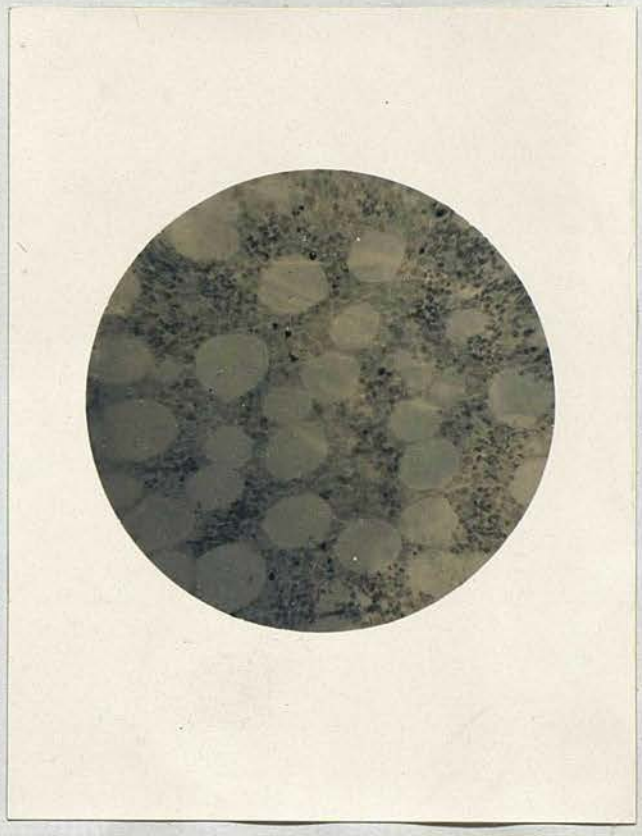
Disappearance of haemogenetic cells.

Fibrillated ring round fat globule.

Absorption of fat globules of the cells.

"Gelatinous material" not so dense as in the chronic form.

Photograph of Oedema of the Marrow inserted for purposes of comparison.



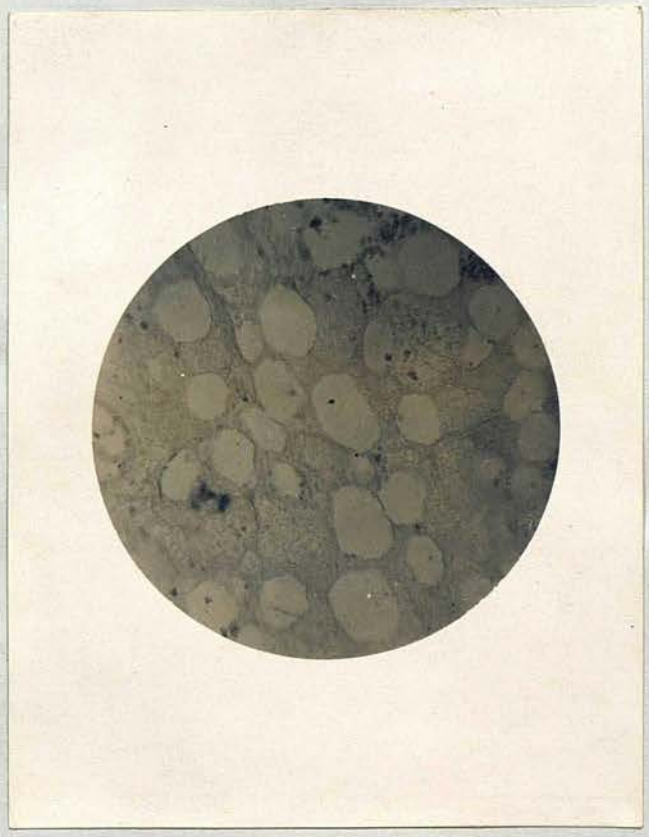
Note the granular appearance and the absence of fibrils.

List of Cases showing Gelatinous Degeneration.

1. Wellmarked fairly acute gelatinous degeneration.

Female, 50 years. (P.M. 30-)

Carcinoma of œsophagus with extreme emaciation and brown pigmentation of skin. Unable to swallow for 11 months prior to death.



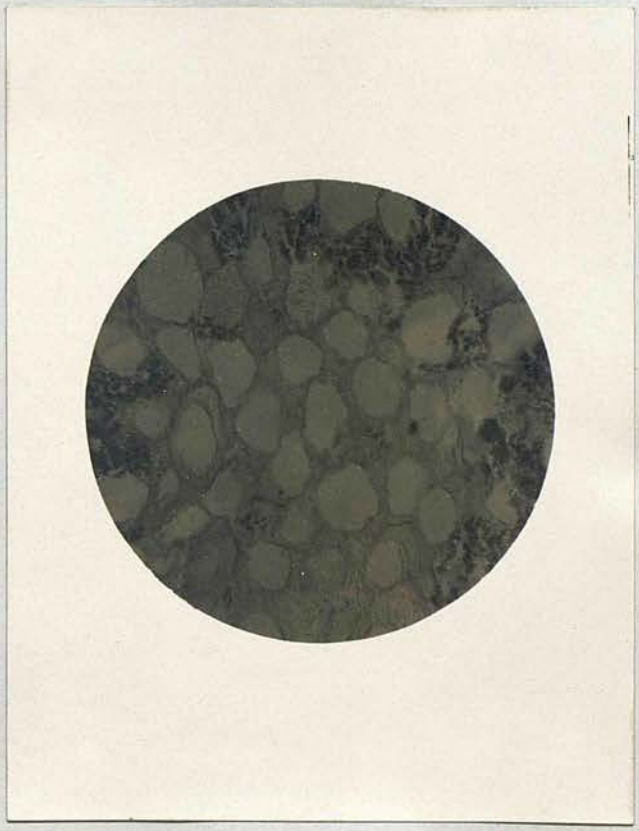
Note the paucity of the hæmogenetic cells, the fibrillated rings round the fat globules and the relative thinness of the homogeneous eosinophil substance.

2. Advanced chronic gelatinous degeneration.

Male, 17 years. (P.M. 37).

Mitral stenosis and simple acute endocarditis of tricuspid valve with extensive pulmonary thrombosis and atheroma of pulmonary veins.

Intermittent attacks of Rheumatic Fever for 12 years and signs of cardiac failure for four years.



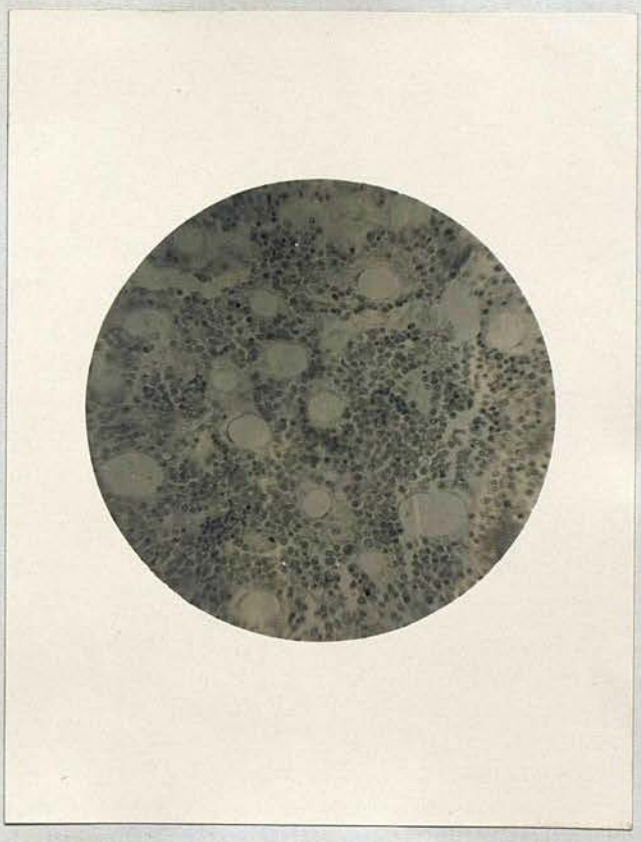
Note the paucity of the haemogenetic cells, the network of fibrils and the denseness of the gelatinous material.

3. Wellmarked fairly acute gelatinous degeneration.

Male, 40 years, (P.M. 72)

Carcinoma arising from the bronchial mucous membrane showing lymphatic spread but no metastases. No tuberculosis.

History of pleurisy a year before death and of cough and loss of weight for last six months.



The haemogenetic cells are fairly numerous. In the upper portion of the photograph the relative thinness of the homogeneous substance is demonstrated.

4. Early gelatinous degeneration in a leucoblastic marrow.

Male, 47 years. (P.M. 107) Retro-pharyngeal cellulitis. History of sepsis for one month and hæmophilia for unknown length of time.

Note the large numbers of hæmogenetic cells of the white series. At the periphery of a few of the fat globules the fibrillated rings are just evident, indicating that the gelatinous degeneration, though early, has been fairly acute.

5. Extremely advanced chronic gelatinous degenerat-
:ion.

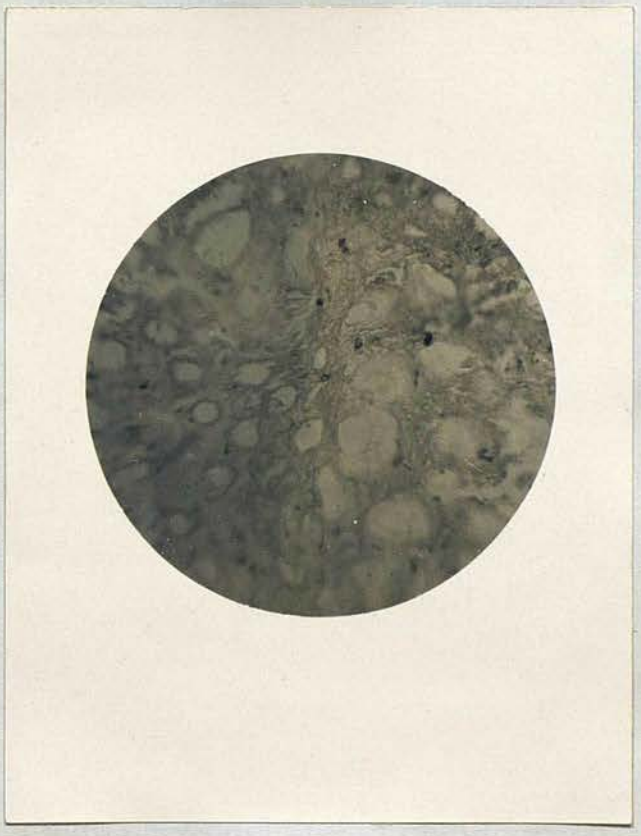
Male, 31 years. (P.M. 111) Carcinoma Simplex of Stomach with metastases in both lungs, liver, mesenteric, bronchial and cervical lymph glands.
Gastric symptoms for 9 years. Continual vomiting and loss of weight for four months.

Note the replacement of the fat cells to an advanced degree by the homogeneous eosin-
:ophil substance

6. Extremely advanced fairly acute gelatinous degeneration.

Male, 64 years. (P.M. 143). Carcinoma of Stomach with acute generalised peritonitis due to obstruction. No metastases.

Gastric symptoms for three months.



The haemogenetic cells have practically all disappeared and the fat cells are fewer and smaller than in health. The fibrillated ring round the fat globules is well demonstrated.

The following technique was employed in each case.

The marrow was fixed in Zenker's solution for 24 hours and than washed in running water for a similar period. When spicules of bone were prominent on the inner aspect of the bone, the tissue was placed for about a fortnight in Perenyi's solution and then rewash-:ed. The tissue was then dehydrated and embedded in paraffin in the usual way. Great care had to be ex-:ercised in avoiding distortion in the changing from one fluid to another.

Sections were then cut on the Cambridge Rocking Microtome. Spicules of bone caused great trouble by spoiling the edges of the razors unless the material had been kept in Perenyi's solution for a long time. The sections were then fixed to the slide. Each had to be treated with iodine and hyposulphite solutions, since the tissue had originally been fixed in Zenker's solut-:ion. Two slides of each portion of marrow were stain-:ed, the one with hæmatoxylin and eosin, and the other with Leishman's stain. During the process of staining, difficulty was experienced as the sections showed a mark-:ed tendency to become detached from the slide in spite of the use of albuminised slides. No. 1 coverslips were used in mounting, to facilitate examination with oil immersion $(\frac{1}{12})$ lenses.

Attempts were made to cut frozen sections after fixation in 10% formalin and washing. After sectioning, however, it was found practically impossible to separate the sections and make them "float out", although various solutions were tried. This was very disappointing, since it was wished to compare the staining reactions of the fat left in gelatinous degeneration with those of the fat of normal marrows.

In one of the marrows definitely found to show gelatinous degeneration (No. 6 of the above series), an attempt to demonstrate mucin was unsuccessful, so corrob-:orating the work of Roger and Josué. A portion of the marrow was fixed in saturated corrosive sublimate solut-:ion and embedded in paraffin in the usual manner.

Sections/

Sections stained with Hoyer's Thionin Method for a quarter of an hour were blue and there was no material stained purple - showing that the presence of mucin could not be demonstrated.

C. AN ACCOUNT OF THE WORK ON THE EXPERIMENTAL PRODUCTION OF GELATINOUS DEGENERATION.

This was performed on lines similar to those previously adopted by Stockman and Charteris.

Buck rabbits were used to eliminate any possible factor due to pregnancy.

The first series of experiments were made on five rabbits whose weights varied between 1,320 grams and 2,470 grams. These were given daily by the mouth, varying amounts of mercuric chloride.

Solutions for the different rabbits were made up with water so that each dose for each rabbit was dis-:solved in ½ cc. The dose was administered from a graduated 1 cc. pipette to the mouth of which was attached a No. 1 soft red rubber catheter. After practice, the catheter was dispensed with and the nozzle of the pipette placed in the rabbit's mouth, the rabbit being held in the box with its back down-:wards.

Each rabbit was weighed frequently and several of them showed a slight terminal loss of weight.

A complete blood examination was made on each rabbit either daily or every second day. Each blood examination/

examination consisted of the estimation of the red blood count, white blood count, hæmoglobin, colour index, differential count and the examination of a stained blood film, and was made at as nearly as poss-:ible the same hour each day, so as to exclude fallacies due to the diurnal variation of the white count.

Control rabbits, i.e., rabbits which did not receive any mercuric chloride, were kept and similar examin-:ations of their blood made. The red blood corpuscles of one and the same control rabbit varied between 4½ million and 6½ million per cubic millimetre. The white blood corpuscles showed waves of leucocytosis (between 9.000 and 18,000 per cubic millimetre) each lasting 10 to 30 days, and associated with a slight relative lymphocytosis. Variations were also noted in the haemoglobin and colour index but no correlation could be traced between any of these variations. The differential counts varied. The average figures were

Polymorphonuclear leucocytes	45%
Lymphocytes	50%
Eosinophils	3.5%
Basophils	1.5%

Examination of the stained film showed the red cells to be anaemic looking compared with the corresponding cells of human blood, and the polymorphonuclear leucocytes contained large amphophil granules, (pseudo-eosinophils).

Note regarding the effect of the administration of corrosive sublimate on the circulating blood.

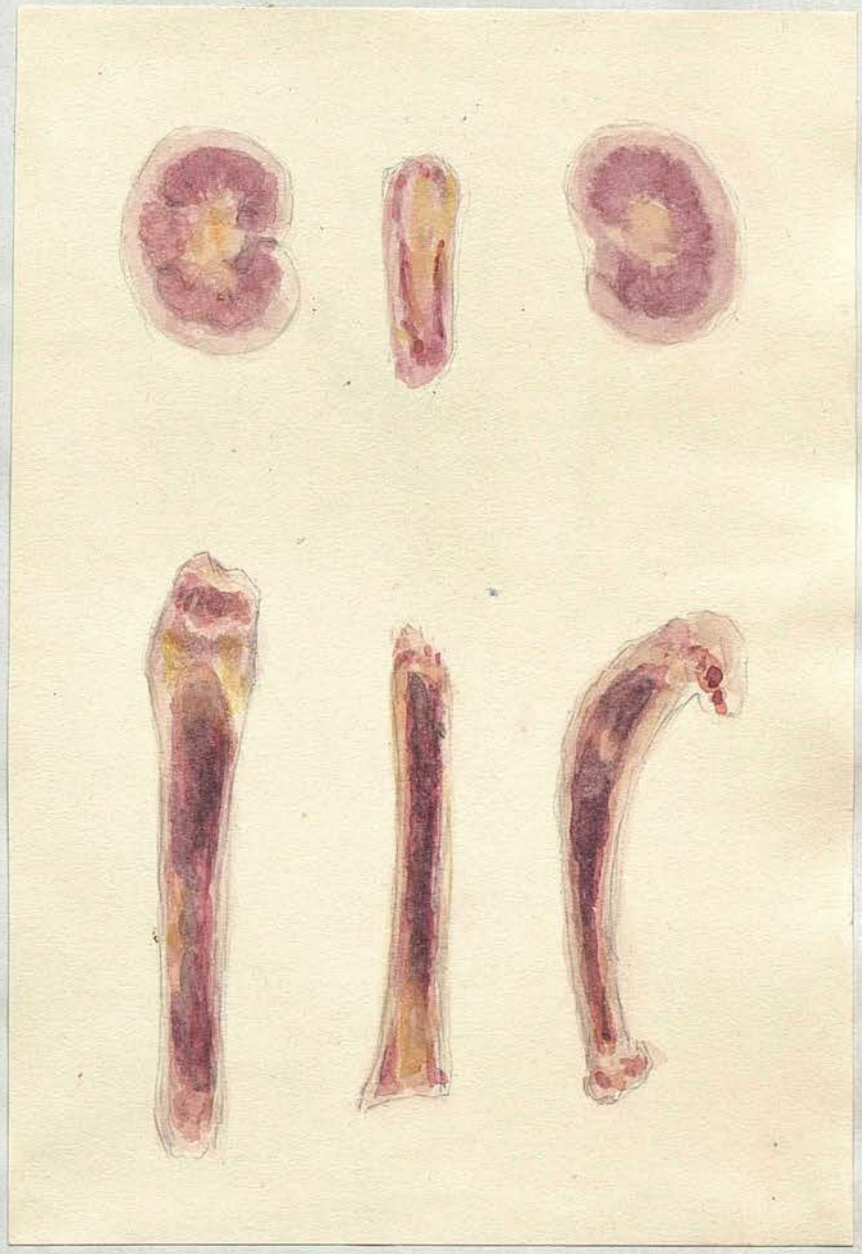
Raimondi found that repeated oral administr-:ation of corrosive sublimate produced a decrease in the number of red blood corpuscles and an increase and pigmentation of white blood corp-:uscles. Keyes and Lindstrœm found that small doses of mercury increased the number of red cells and the haemoglobin in man, while large doses diminished them. Schlesinger found an increase of red cells and hæmoglobin in rabbits and dogs after small doses of corrosive sub-:limate. Stockman and Charteris, however, did not find an increase in these, and they ascribe their results to their use of comparatively large doses.

In none of the rabbits used in this in-:vestigation were there noted any steady increase or decrease in the red count, the white count , the hæmoglobin, the colour index or the differential count, or any marked difference in the appearances of the stained film.

Since Rabbit No. 1. eventually showed gelatinous degeneration of the marrow, the results of its daily blood examinations while alive are presented in tabular form on pages 27 and 28.

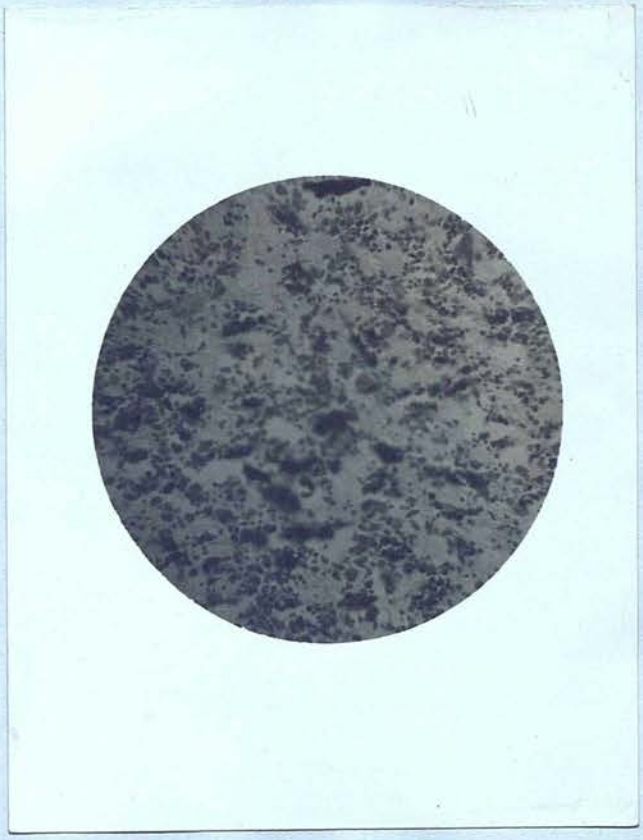
In examining the bone marrows of rabbits it is of great importance to remember that specimens taken from the shafts of the long bones is comparable to the red marrow in the ends of the long bones in humans.

Rabbit No. 1. received 5 mg. of mercuric chloride daily for 51 days. It seemed quite well until the forty-seventh day when one of its ears was bitten by another rabbit by whom it was eventually killed. To-:wards the end it lost weight slightly, - about a twentieth of its original weight in all. At the autopsy, the marrow was found to be completely alter-:ed to a greyish-yellow gelatinous substance not un-:like chicken-fat, which microscopically gave the typical appearances of acute gelatinous degeneration. in widespread areas. (See pages 25 and 26). The fibrillar network was well seen, but I could not con-vince myself that I saw the small cells with rounded nuclei of which the fibrils are supposed to be the processes. The stomach and intestines showed catarrh, which, presumably was due to the direct action of the corrosive sublimate. The kidney tubules showed advanced acute parenchymatous degener-:ation, - out of proportion to the glomerular changes but still very much less severe than the necrosis of the acute form of corrosive sublimate poisoning. The remaining internal organs showed congestion and toxic changes.



Rabbit No.1. Bone Marrow and Kidneys.

Photograph of the Marrow of Rabbit No. 1.



This portion of marrow was removed from the middle of the shaft of the right femur, where in healthy rabbits typical red marrow is found. The haemogenetic cells are therefore greatly reduced in number. No fat at all is seen in this preparation and the thinness of the gelatinous material is sufficient to warrant the diagnosis of Acute Gelatinous Degeneration.

RABBIT No. I.

DAY OF EXPT.	DATE	R. B. C.		Hb. (APPROXIMATE)		C.I.	W. B. C.		NUCLEATED R.B.C.	POIKYLO-CYTOSIS.	ANISO-CYTOSIS.	PUNCTATE BASOPHILIA	POLY-CHROMATO-PHILIA.	DIFFERENTIAL W.B.C. COUNT.					WEIGHT IN GRAMS.
		NUMBER PER Cu. MM.	%	Actual %age	%age RELATIVE TO 80	%Hb / % RBC	NUMBER PER Cu. MM.	%age						P.	SL.	LL.	E.	B.	
-	28. 2. 27.	4,800,000	4,950,000 =100%	78	100	1·0	6,400	7,000 =100%	-	-	-	-	-	40	30	24	4	2	2,000
-	3. 3. 27.	5,100,000		82			7,600		-	-	-	-	-	42	31	22	4	1	1,950
1	5. 3. 27.	6,000,000	121	90	112·5	·93	7,900	113	-	-	-	-	-	46	31	19	3	1	2,050
2	6. 3. 27.	5,750,000	116	90	112·5	·97	6,800	97	-	-	-	-	-	47	29	21	2	1	2,000
3	7. 3. 27.	5,730,000	116	90	112·5	·97	6,600	94	-	-	-	-	-	43	30	21	4	2	1,970
4	8. 3. 27.	6,010,000	121	90	112·5	·93	7,800	111	-	-	-	-	-	49	28	20	3	0	2,120
5	9. 3. 27.	5,710,000	115	90	112·5	·98	8,200	117	-	+	-	-	-	45	30	19	4	2	2,030
6	10. 3. 27.	5,700,000	115	90	112·5	1·00	9,600	137	-	-	-	-	-	41	31	21	5	2	1,990
7	11. 3. 27.	5,320,000	107	85	106·25	1·00	10,200	146	-	-	-	-	-	38	30	27	3	2	2,210
8	12. 3. 27.	4,900,000	99	80	100·0	1·00	15,600	223	-	-	-	-	-	37	31	27	4	1	2,140
9	13. 3. 27.	5,000,000	101	80	100·0	1·00	19,300	276	-	-	-	-	-	35	29	30	4	2	2,120
10	14. 3. 27.	5,100,000	103	80	100·0	·99	18,600	266	-	-	-	-	-	35	30	30	4	1	2,130
11	15. 3. 27.	4,750,000	96	80	100·0	1·04	18,200	260	-	+	-	-	-	33	32	29	4	2	2,300
12	16. 3. 27.	4,790,000	97	80	100·0	1·03	16,400	234	-	-	-	-	-	34	31	29	4	2	2,180
13	17. 3. 27.	5,300,000	107	80	100·0	·93	11,400	163	-	+	-	-	-	36	30	29	5	0	2,220
14	18. 3. 27.	5,120,000	103	80	100·0	·97	12,300	176	-	-	-	-	-	38	31	26	3	2	2,120
15	19. 3. 27.	5,050,000	102	80	100·0	1·00	13,600	194	-	-	-	-	-	41	35	20	3	1	2,130
16	20. 3. 27.	4,900,000	99	80	100·0	1·00	14,400	206	-	-	-	-	-	41	37	19	2	1	1,980
17	21. 3. 27.	4,950,000	100	80	100·0	1·00	17,900	256	-	-	-	-	-	34	32	27	5	2	1,970
18	22. 3. 27.	5,100,000	103	80	100·0	1·00	18,600	266	-	-	-	-	-	33	31	30	5	1	2,030
19	23. 3. 27.	4,990,000	101	80	100·0	1·00	13,500	193	-	+	-	-	-	35	32	29	3	1	1,990
20	24. 3. 27.	4,980,000	101	80	100·0	1·00	13,400	191	-	-	-	-	-	39	35	23	2	1	1,990
21	25. 3. 27.	4,120,000	83	70	87·5	1·05	16,200	231	-	+	+	-	-	41	36	19	3	1	2,020
22	26. 3. 27.	3,710,000	75	65	81·25	1·08	19,200	274	-	+	-	-	-	44	37	13	4	2	2,030
23	27. 3. 27.	4,230,000	86	70	87·5	1·03	18,400	263	-	-	-	-	-	42	35	19	3	1	1,990
24	28. 3. 27.	4,440,000	90	70	87·5	·97	16300	233	-	-	-	-	-	43	32	19	4	2	2,000

RABBIT No. 1. - continued.

DAY OF EXPT:	DATE.	R.B.C. NUMBER PER CU: MM:	R.B.C. %	Hb (APPROXIMATE) ACTUAL % age	Hb (APPROXIMATE) RELATIVE TO 80.	C.I. % HB / % R.BC.	W.B.C. NUMBER PER CU: MM:	W.B.C. % age.	NUCLEATED R.B.C.	POIKYLO: CYTOSIS.	ANISO: CYTOSIS.	PUNCTATE BASOPHILIA	POLY' CHROMATO: PHILIA.	DIFFERENTIAL W.B.C. COUNT. P.	S.L.	L.L.	E.	B.	WEIGHT IN GRAMS.
25	29. 3. 27.	4,450,000	90	70	87·5	·97	10,600	151	-	-	-	-	-	46	27	23	3	1	2,010
26	30. 3. 27.	4,750,000	96	75	93·75	·98	9,800	140	-	-	-	-	-	47	28	22	2	1	2,030
27	31. 3. 27.	4,750,000	96	75	93·75	·98	11,600	166	-	-	-	-	-	43	26	25	4	2	2,020
28	1. 4. 27.	5,100,000	103	80	100·0	·97	11,800	169	-	-	-	-	-	40	28	27	3	2	2,000
29	2. 4. 27.	5,450,000	110	85	106·25	·97	13,400	191	-	-	-	-	-	37	29	29	4	1	2,020
30	3. 4. 27.	4,930,000	100	80	100·0	1·00	14,000	200	-	-	-	-	-	33	31	30	4	2	1,990
31	4. 4. 27.	4,950,000	100	80	100·0	1·00	12,700	181	-	-	-	-	-	34	31	29	4	2	1,970
32	5. 4. 27.	4,850,000	98	80	100·0	1·02	11,400	163	-	+	-	-	-	38	29	28	4	1	2,000
33	6. 4. 27.	4,300,000	87	70	87·5	1·01	14,900	213	-	+	-	-	-	39	32	25	3	1	2,010
34	7. 4. 27.	4,150,000	84	70	87·5	1·04	15,000	214	-	+	-	-	-	42	33	20	4	1	1,980
35	8. 4. 27.	4,660,000	94	75	93·75	1·00	14,300	204	-	-	-	-	-	41	31	23	4	1	1,960
36	9. 4. 27.	4,850,000	98	80	100·0	1·02	13,800	197	-	-	-	-	-	47	29	21	2	1	1,890
37	10. 4. 27.	5,100,000	103	80	100·0	·99	12,900	184	-	-	-	-	-	44	29	23	3	1	1,900
38	11. 4. 27.	5,230,000	106	85	106·25	1·00	11,000	157	-	-	-	-	-	42	30	23	4	1	1,910
39	12. 4. 27.	5,550,000	112	85	106·25	1·00	11,400	163	-	-	-	-	-	45	31	19	3	2	1,880
40	13. 4. 27.	5,540,000	112	85	106·25	·95	9,800	140	-	-	-	-	-	47	32	17	3	1	1,860
41	14. 4. 27.	5,600,000	113	85	106·25	·95	7,600	109	-	-	-	-	-	46	31	19	3	1	1,840
42	15. 4. 27.	5,310,000	107	85	106·25	1·00	7,700	110	-	-	-	-	-	49	32	16	3	0	1,900
43	16. 4. 27.	5,010,000	101	80	100·0	1·00	7,800	111	-	-	-	-	-	47	33	17	2	1	1,870
44	17. 4. 27.	5,620,000	113	90	112·5	1·00	11,300	161	-	-	-	-	-	42	35	19	3	1	1,960
45	18. 4. 27.	5,930,000	120	90	112·5	·94	15,400	220	-	-	-	-	-	38	35	21	4	2	2,000
46	19. 4. 27.	5,840,000	118	90	112·5	·94	18,500	264	-	-	-	-	-	37	36	21	4	2	1,890
47	20. 4. 27.	5,010,000	101	80	100·0	1·00	17,700	253	-	-	-	-	-	35	35	25	4	1	1,950
48	21. 4. 27.	5,630,000	114	85	106·25	·93	17,000	243	-	-	-	-	-	34	33	27	4	2	1,860
49	22. 4. 27.	5,010,000	101	80	100·0	1·00	12,300	176	-	-	-	-	-	40	35	20	3	2	1,870
50	23. 4. 27.	4,830,000	98	80	100·0	1·02	11,400	163	-	-	-	-	-	44	31	21	3	1	1,850

Rabbit No. 2. received 5 mg. of mercuric chloride daily for fifty days, after which 50 mg. per day was given for two days and then all doses were stopped. The rabbit died on the fifty-sixth day. Neither macroscopic nor microscopic evidence of gelatinous degeneration was found. Otherwise the findings in the internal organs were similar to those found in rabbit No. 1.

Rabbit No. 3. received 10 mg. of mercuric chloride daily for 11 days when it was accidentally killed by a subdural haemorrhage caused by falling off a table. The marrow showed no changes and beyond slight cloudy swelling of the internal organs no lesion was found.

Rabbit No.4. received 10 mg. of mercuric chloride daily for 51 days. On the forty-ninth day the right ear was bitten by another rabbit. On each of the fifty-second and fifty-third days, doses of 75 mg. were given and the rabbit died on the fifty-fourth day. The marrow showed no macroscopic evidence of gelatinous degeneration, and microscopically, the granularity and absence of fibrils indicated oedema. The findings in the other organs were similar to those of rabbits Nos. 1 and 2.

Rabbit No. 5.was given 50 mg. of mercuric chloride per day for four days after which it died. The Bone Marrow was unchanged.

Since the only one of these five rabbits to have shown gelatinous degeneration of the marrow had received 5 mg. daily, a further series of experiments was performed in which each of five rabbits received a similar daily dose. These rabbits were numbered 6 to 10. Unfortunately, not one of them developed the gelatinous degeneration.

Rabbit No. 6.died on the 38 th. day. There was considerable congestion of the marrow and the usual toxic changes in the other organs.

Rabbit No. 7.died on the 40 th. day. It pre-:sented wellmarked œdema of the marrow. Scattered fairly regularly throughout the marrow were fairly large pale cells. They stained very faintly with haematoxylin and their cytoplasm was delicate and vacu-:olated. Each possessed a single small nucleus usually situated near the centre of the cell. These cells resembled endothelial cells but their nuclei were smaller and denser and their cytoplasm was less deeply stained. (See photograph on p.31. The paleness of these cells renders them difficult to be seen in the photograph).

Photograph of the Marrow of Rabbit No. 7.

This portion of marrow was removed from the middle of the shaft of the right femur. In the absence of fibrils the granularity is indicative of oedema. Some curious very faintly-staining vacuolated cells were observed, one being just visible in the centre of the photograph. No reference to them has been found in the literature. They may play some part in the removal of the fat in the early stages of gelatinous degeneration.

The remaining Rabbits,- Nos.8,9 and 10. were all killed on the 117th. day. Numbers 8 and 9 showed oedema of the marrow and number 10 showed slight congestion. In none was there evidence of gelatinous degeneration.

Owing to restrictions under the Home Office regulations for animal experiments, the work of Jackson in producing gelatinous degeneration by starv-:ation could not be confirmed - nor could operations be performed for the removal of bone marrow for exam-:ination at various stages in the courses of mercuric chloride.

D. CONCLUSIONS.

1. Gelatinous Degeneration is a comparatively rare condition, being found in only six out of over a hundred and fifty cases in the postmortem room.

2. Gelatinous Degeneration may be present without being recognisable to the naked-eye. Often its presence can be proven only after microscopic examination.

3. Gelatinous Degeneration can be produced by the oral repeated administration of small doses of mercuric chloride. In addition, however, other factors are probably necessary for its production since the marrows of the rabbits given the same or larger doses than the one which developed the degeneration, remained unaffected. Otherwise, the reaction of individual rabbits to mercuric chloride must vary enormously.

4. Blood Changes. There may not be any blood changes recognisable clinically in (at least) acute gelatinous degeneration. This was shown by Rabbit No.1.

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E. ACKNOWLEDGMENTS

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